

Examiner asked Applicants to make these deficiencies of record in a written Response, and, accordingly, they are set forth below.

**A. Zhang Does Not Provide A Basis For A Prima Facie Case Of Obviousness Because It Does Not Teach Or Suggest Every Limitation Of The Rejected Claims**

To set forth a *prima facie* case of obviousness of a claim over a reference, the Examiner must show that the reference discloses, teaches or suggests every limitation of the claim. See MPEP ¶ 2143.03.

Applicants respectfully assert that Zhang does not disclose, teach or suggest every limitation of the rejected claims, including independent claims 1, 19, and 32.

1. Claims 1 and 32

With respect to independent claims 1 and 32, Zhang's dosage forms do not adjust local environment to promote dissolution. Briefly, all Zhang dosage forms include a solid solution portion containing a drug. If an ionized form of the drug is present, the concentration of the ionized form is adjusted *in vitro* before the solid solution is formed. See, e.g., col. 8, lines 7-8 ("The pH of wet granulated particles is adjusted so that the drug is ionized . . . [emphasis added]."); and cols. 11-12, Example 1, particularly, col. 12, lines 1-2 (teaching *in vitro* mixing of piroxicam and sodium hydroxide in water, thus adjusting the concentration of the ionized form before forming a solid solution). Once the drug is in the solid solution of the Zhang dosage form, the concentration of the ionized form remains the same until the dosage form is administered. Upon administration, no adjustment of the local environment takes place. Instead, the drug, which is already

dissolved in the solid solution, is forced to dissolve into the body fluid due to the nature of the solid solution. See, e.g., col. 8, lines 54-56 ("[T]he dissolution rate is no longer determined by the characteristics of the drug itself, but by the dissolution profile of the solid solution [emphasis added]."). See also col. 8, lines 56-59 ("... solid solution matrices usually dissolve quickly to release the drug in the oral cavity.").

Thus, at a minimum, *Zhang* does not teach or suggest "adjusting a localized environment of the active ingredient to promote dissolution," as recited in independent claims 1 and 32. At least on this ground, Applicants respectfully maintain that *Zhang* does not provide a basis for a *prima facie* case of obviousness of claim 1 or claim 32.

## 2. Claim 19

With respect to independent claim 19, none of the *Zhang* dosage forms contain more than one pH-adjusting substance under any remotely plausible interpretation. Furthermore, nothing in *Zhang* suggests any possible advantage that would flow from using more than one pH-adjusting substance. Therefore, at a minimum, *Zhang* clearly does not teach or suggest a dosage form containing "a first pH adjusting substance" and "a second pH adjusting substance" for promoting dissolution and absorption, respectively, as recited in claim 19.

At least on this ground, Applicants respectfully maintain that *Zhang* does not provide a basis for a *prima facie* case of obviousness of claim 19.

**B. Zhang Does Not Provide A Basis For A Prima Facie Case Of Obviousness Because It Does Not Motivate One Skilled In The Art To Modify Zhang In The Direction Of The Rejected Claims**

To set forth a *prima facie* case of obviousness of a claim over a reference, there must be a teaching, suggestion or motivation to modify the reference in the direction of the claim. See MPEP ¶ 2143.01. Furthermore, the teaching of the reference must be taken as a whole. See, e.g., MPEP ¶ 2141.02. The prior art must be considered in its entirety, including disclosures that teach away from the claim. See *id.*

1. Claims 1 and 32

*Zhang* does not provide one skilled in the art with a motivation or a suggestion to modify the *Zhang* dosage forms in the direction of claim 1 or claim 32. To the contrary, *Zhang* repeatedly emphasizes the advantage of higher in-tablet stability of the ionized form in the formulation. See, e.g., col. 5, line 6; col. 8, line 2; and col. 9, lines 22-32. Thus, taken as a whole, *Zhang* clearly suggests adjustment/formulation of the solid solution portion, for example, to the desired pH rather than adjustment of the local environment. Therefore, *Zhang*, considered as a whole, teaches away from claims 1 and 32.

Applicants respectfully maintain that the lack of motivation and the teaching away further show *Zhang's* deficiency as a basis for a *prima facie* case of obviousness with respect to claim 1 or claim 32.

2. Claim 19

*Zhang* does not provide a motivation or a suggestion to modify its dosage forms in the direction of claim 19. As set forth above, claim 19 requires presence of more than one pH-adjusting substance. Why one skilled in the art would be

motivated to modify the *Zhang* dosage form at all when faced with *Zhang's* teaching of a completely different (and allegedly successful) dissolution mechanism? Further, as described herein above, *Zhang's* emphasis on the stability advantages of its formulation methodology teaches away from claim 19.

Applicants respectfully maintain that the lack of motivation and the teaching away further show *Zhang's* deficiency as a basis for a *prima facie* case of obviousness with respect to claim 19.

### C. Conclusion

Thus, Applicants maintain that the Examiner has not set forth a *prima facie* case of obviousness of claims 1, 19, and 32. It should be noted, and the Examiner is asked to take into account, that the preceding arguments are directed and limited toward *Zhang's* deficiencies as the basis for a *prima facie* case of obviousness.

Applicants state that dependent claims 2-18, 20-31, and 33-46 do not stand and fall with independent claims 1, 19, and 32, respectively. However, in the absence of *prima facie* obviousness of the independent claims, no additional arguments are necessary with respect to dependent claims 2-18, 20-31 and 33-46. *Zhang* cannot provide the basis for a *prima facie* case of obviousness of the dependent claims if the corresponding independent claims are not *prima facie* obvious.

In view of the foregoing remarks and the understandings reached at the November 5 interview, withdrawal of the rejection and allowance of the pending claims are respectfully requested.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited. If, however, for any reason the Examiner does not believe that such action can be taken at this time, the Examiner is respectfully requested to contact the undersigned counsel at (908) 654-5000 in order to overcome any additional objections.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: November 12, 2002

Respectfully submitted,

By ES Pergament  
Edward D. Pergament  
Registration No.: 43,346  
LERNER, DAVID, LITTENBERG,  
KRUMHOLZ & MENTLIK, LLP  
600 South Avenue West  
Westfield, New Jersey 07090  
(908) 654-5000  
Attorneys for Applicant